Role of HDAC in human stem cells pluripotentiality and differentiation

Grant Award Details

Role of HDAC in human stem cells pluripotentiality and differentiation

Grant Type: SEED Grant

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Investigator:

Name:	Eric Verdin
Institution:	Gladstone Institutes, J. David
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $590,997

Status: Closed

Grant Application Details

Application Title: Role of HDAC in human stem cells pluripotentiality and differentiation

Public Abstract:

Stem cells are able to develop into most of the specialized cells and tissues of the body and therefore have the potential to replace diseased cells with healthy functioning ones. It is the hope of the scientific and medical communities that the use of stem cell based therapies to treat diseases such as Alzheimer's disease, diabetes, heart disease and other degenerative conditions will one day be routine. Because this research field is still in its infancy, a number of scientific challenges must be overcome before promise of stem cells can be harnessed. In particular, we need to increase our understanding of the growth conditions, cellular biology and genetic events involved in stem cell survival and differentiation are key. While more than 100 distinct stem cell lines have been derived, less than 20 are available in sufficient quantities for research purposes and of these, only a very limited number have studied with respect to understanding how stem cells grow and develop into target cells. Clearly there is a great need to study more cell lines to allow comparative analysis of growth conditions, signaling and gene expression processes. These studies will help clarify how these cells can be grown to sufficient quantities to be used clinically and will also help determine at stage these cells have maximum therapeutic potential.

We are interested in understanding in molecular details two key properties of stem cells. First, self renewal is defined as the ability of stem cells to divide indefinitely, in contrast to non-stem cells which are limited in their ability to divide. Second, pluripotentiality refers to the ability of stem cells to differentiate in all cell types that are present in an adult organism. There is growing evidence that these two properties of stem cells are controlled at the central level via the interplay of cellular factors that control the transfer of DNA into RNA. Several key transcription factors have been identified that are unique to stem cells. Our laboratory has specialized during the last 20 years in the study of a family of proteins called histone deacetylases that control the activity of many transcription factors. However, no data exist on the possible role of these proteins in the self renewal and pluripotentiality of stem cells. We propose a series of experiments that will explore the role of histone deacetylases in these critical properties of stem cells.

This information will ultimately advance our efforts at generating stem cells with therapeutic potential for use in the clinic.

Statement of Benefit to California:

Human stem cells have the potential to replace diseased or dysfunctional cells with healthy functioning ones. This new technology represents one of the most exciting medical advances in history. Early results from stem cell therapy trials have prompted significant optimism in the scientific community that these therapies will one day be used routinely to cure a series of diseases ranging from Alzheimer's disease to diabetes. Before the potential for this new technology can be realized, there remains much to be learned about the biology of stem cells including how stem cells differentiate to different cell types, what are the factors that trigger differentiation and contribute to their viability, etc. Our studies plan to explore the role of human histone deacetylases in human embryonic stem cell biology. Human histone deacetylases are a family of protein that regulate the expression of specific genes in human embryonic stem cells and in more differentiated adult cells. These studies will provide important insights into how histone deacetylases contributes to embryonic stem cell biology and their differentiation. Understanding these basic mechanisms will lay the foundation to therapies for numerous diseased that effect the citizens in this state and the world.
